IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BOARD OF APPEALS AND INTERFERENCES

Applicant: Hilfinger, J, et al.

Serial No.: 10/706,738 Group Art Unit: 1635

Filed: November 12, 2003 Examiner: Richard Schnizer

For: METHODS AND COMPOSITIONS OF GENE DELIVERY AGENTS FOR SYSTEMIC AND LOCAL THERAPY

APPELLANTS' APPEAL BRIEF UNDER 37 CFR §41.37

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

As required under § 41.37(a), this brief is filed within two months of the Notice of Appeal filed in this case on April 2, 2007, and is in furtherance of said Notice of Appeal.
The fees required under § 41.20(b)(2) are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.
This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1205.2:

I.	Real Party In Interest
II	Related Appeals and Interferences
III.	Status of Claims
IV.	Status of Amendments
V.	Summary of Claimed Subject Matter
VI.	Grounds of Rejection to be Reviewed on Appeal
VII.	Argument
VIII.	Claims
Appendix A	Claims
Appendix B	Evidence
Appendix C	Related Proceedings

I. Real Party in Interest

The real party in interest in this appeal are the co-assignees, TSRL, Inc. and The Regents of the University of Michigan.

II. Related Appeals and Interferences

Appellant is aware of no appeals or interferences pending or otherwise related to the present appeal.

III. Status of the Claims

The present application was initially filed with 7 claims. Claims 8-30 were added by amendment. Claims 1-7, 17-18, 21, 23, 25, and 28-29 have been canceled. Claims 8-16, 19, 20, 22, 24, 26, 27, and 30 are pending, finally rejected, and under appeal. Claims 8 and 20 are the only pending independent claims.

IV. Status of Amendments Filed Subsequent Final Rejection

No after-final amendments have been filed.

V. Summary of the Claimed Subject Matter

Independent claim 8 relates to a method of delivering nucleic acid to a target cell of a subject by administering a conjugating nucleic acid complex wherein the conjugating agent comprises A–R_1–Q–Z (page 9, lines 15-16; page 11, lines 1-4) wherein A-R^1 is a cholestanol, coprostanol, glycocholic acid, chenodeoxycholic acid, desoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, or taurochenodeoxycholic acid (page 10, lines 3-6), Q is a sulfur or oxygen (page 9, line 23 - page 10, line 1), and Z is a polyionic peptide (page 10, line 2). Claim 9 relates to the oral administration of the nucleic acid to a target cell of a subject of claim 8 (page 15, line 7). Claim 10 and 11 relate to the nucleic acid of the complex of claim 8 being expressed as a protein in the target cells, and the protein thereafter being execreted,

respectively (page 14, lines 17-21). Claim 12 relates to a Markush group of proteins per claim 8 (page 11, lines 20-23). Claim 13 relates to a Markush group of nucleic acids types per claim 8 (page 7, lines 19-20). Claim 14 relates to administration per claim 8 as part of a pharmaceutical composition (page 15, line 6). Claim 15 relates to the inclusion of an active therapeutic compound in the composition of claim 14 (page 18, line 23 – page 19, line 3). Claim 16 is a Markush group of active therapeutic compounds per claim 15 (page 18, line 23 – page 19, line 3). Claim 19 relates to the target cells being gastrointestinal cells (page 3, lines 2-3)

Independent claim 20 relates to a nucleic acid delivery composition comprising a conjugating nucleic acid complex having the formula $A–R_1–Q–Y–Z$ (page 9, lines 15-16) wherein $A\text{-}R_1$ is a cholestanol, coprostanol, glycocholic acid, chenodeoxycholic acid, desoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, or taurochenodeoxycholic acid (page 10, lines 3-6), Q is a sulfur or oxygen (page 9, line 23 - page 10, line 1), Y is a linker peptide having a negative, neutral, or positive charge (page 10, lines 1-2), and Z is a polyionic peptide (page 10, line 2). Claim 22 relates to the cholesterol derivative of claim 20 being deoxycholic acid (page 10, lines 4-6). Claim 24 relates to the Q of claim 20 being oxygen (page 10, line 1). Claim 26 relates to Z of claim 20 being polycationic (page 12, line 17). Claim 27 relates to Z of claim 26 having at least 6 residues (page 12, lines 19-20). Claim 30 relates of a commercial package per claim 8 with usage instructions and so finds like support with claim 8.

VI. Grounds of Objection/Rejection to Be Reviewed on Appeal

A. The rejection of claims 8-10, 13, 14, 19, 20, 22, 24, 26, 27, and 30 under 35 U.S.C. § 103(a) over Niedzinski et al (Lipids 35(7): 721-727, 2000), hereinafter referred to as Niedzinski, in view of Keener et al (US Patent 6,627,197), hereinafter referred to as Keener, and

Gebeyehu et al (US Patent 6,075,012), hereinafter referred to as Gebeyehu, and is detailed in Paper No. 20070907.

B. The rejection of claims 15 and 16 under 36 U.S.C § 103(a) as to the base claim and in further view of Perrie et al (J. Liposome Res. 12(1&2): 185-197, 2002), hereinafter referred to as Perrie and is detailed in Paper No. 20070907.

C. The rejection of claims 11, 12, 15, and 16 under 35 U.S.C. § 103(a) as to the base claim and in further view of Kitadai et al (Brit. J. Cancer 81(14): 647-653, 1999), hereinafter referred to as Kitadai and is detailed in Paper No. 20070907.

VII. Argument

The Examiner's Position

The examiner based his rejection of claims 8-10, 13, 14, 19, 20, 22, 24, 26, 27, and 30 as obvious under 35 U.S.C. § 103(a) over Niedzinski, in view of Keener, and Gebeyehu.

Niedzinski is cited as teaching "cholic acid conjugates comprising a polyamine DNA binding domain, their use to protect DNA from degradation in the gastric system, and their use to deliver plasmids to NIH 3T3 cells in vitro." (Paper No. 20070907, pg. 3.) The Examiner in an Office communication dated September 17, 2007 states that: "It would have been obvious to one of skill in the art at the time of the invention to substitute any hydrophobic bile acid or cholesterol derivative for the cholic acid of Niedzinski." (Paper No. 20070907, pg. 4).

Keener is cited as teaching "the use of bile acids, and cholesterol derivatives generally, as hydrophobic conjugates to aid in the cellular entry of a conjugated peptide." (Paper No. 20070907, pg. 3.) Examiner bridges Niedzinski with Keener because "Niedzinski considered his conjugation technique to be applicable to a variety of bile acids (see last sentence of column 1 on

page 724), and it was clear that it could be applied to either the C3 hydroxyl (sic), so the presence of a carboxyl group was not required." (Paper No. 20070907, pg. 3) (emphasis added).

Gebeyehu is cited as teaching reagents and methods for intracellular delivery of nucleic acids that are cationic lipids with the formula ABZ where the A represents a steroid such as cholic acid, stigmasterol, or ergosterol, B represents a linker, and Z may be a nucleic acid binding domain such as a polyamine or polycationic peptide. (Paper No. 20070907, pg. 4.) Examiner's position is that "[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a nucleic acid binding peptide [of Gebeyehu] for the nucleic acid binding polyamine of Niedzinski because these nucleic acid binding moieties were recognized in the art as equivalents. (Id. at 5.) Gebeyehu is further referred on page 11 of Paper No. 20070907:

> Regarding Gebeyehu, Applicant argues that the reference does not teach or suggest the use of any cholesterol derivative other than stigmasterol, ergosterol, or cholic acid. Gebeyehu was not relied upon to teach any derivative other than these. The cholesterol derivatives are taught by Niedzinski and Keener. Gebeyehu taught the use of nucleic acid binding domains, such as a polyamine or a polycationic peptide, in combination with a steroid such as cholic acid, stigmasterol, or ergosterol, and a linker. Clearly polyamines and cationic peptides were recognized in the art as equivalents as DNA binding domains in delivery compositions, such that it would have been obvious to substitute one for the other in the invention of Niedzinski as modified by Keener.

Thus, Gebeyehu is cited merely for the proposition that polyamines and cationic peptides are art recognized equivalents. (*see also* Paper No. 20070907, pg. 5.)

The examiner based his rejection of claims 15 and 16 as obvious under 35 U.S.C. § 103(a) over Niedzinski, in view of Keener, and Gebeyehu, in further view of Perrie. The base references are cited as lacking any teaching of protein secretion from target cells or claiming the composition as a therapeutic compound. (Paper No. 20070907, pg. 6.) Perrie is cited as teaching "oral intragastric delivery of cationic liposome comprising nucleic acids encoding the S (small)

region of the hepatitis B surface antigen (HBsAg) . . . [wherein] . . . DNA vaccines encoding HBsAg were formulated with cationic lipids (DOTAP) and administered orally." (Paper No. 20070907, pg. 6.) The examiner believes Niedzinski taught "that the lipid could be substituted for, or added to, such cationic lipids as DOTAP," and the Niedzinski compounds are art recognized equivalents of cationic lipids. (Paper No. 20070907, pg. 7.) Claims 15 and 16 are present in the rejection because of Examiner's belief that the nucleic acid of Perrie is a therapeutic product because it is "antibiotic in nature" such that it induces "an immune response against hepatitis B virus." (Paper No. 20070907, pg. 7.)

The Examiner based his rejection of claims 11, 12, 15, and 16 as obvious under 35 U.S.C. § 103(a) over Niedzinski, in view of Keener, and Gebeyehu, in further view of Kitadai. The base references are cited as not teaching secretion of an expressed protein or a composition comprising a therapeutic compound. Kitadai is cited as teaching an expression vector encoding the secreted protein interleukin-8 that was transfected into cells using the cationic lipid LIPOFECTIN (DOTMA/DOPE). (Paper No. 20070907, pg. 8.)

Appellant's Position

A. Rejection of Claims 8-10, 13, 14, 19, 20, 22, 24, 26, 27, and 30.

Argument 1: Niedzinski in view of Keener fails to render the A-R_1 moiety obvious in the instant inventive method.

Examiner bridges Niedzinski with Keener because "Niedzinski considered his conjugation technique to be applicable to a variety of bile acids (see last sentence of column 1 on

page 724), and it was clear that it could be applied to either the C3 hydroxyl (sic), so the presence of a carboxyl group was not required." (Paper No. 20070907, pg. 3) (emphasis added). That a conjugation technique is amenable to multiple bile acids does not suggest to a person having ordinary skill in the art that multiple bile acids are suitable for delivering nucleic acid to target cells.

As was recently articulated by the Federal Circuit, for a case of *prima facie* obviousness to be found for chemical matter, "[i]n addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of 'adequate support in the prior art' for the change in structure." Takeda Chem. Indus., Ltd. v. Alphapharm Pty, LTD, 83 USPQ2d 1169, 1174 (Fed. Cir. 2007). The court further made expressly clear that "in order to find a prima facie case of unpatentability in such instances, a showing that the 'prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention' was also required." Id. (quoting In re Deuel, 51 F.3d 1552, 1558 (Fed. Cir. 1995) (internal references omitted). The court clarified that this test for chemical compounds is "consistent with the principles enunciated in KSR." Id. (citing KSR Int'l Co. v. Teleflex, Inc., 127 S. Ct. 1727 (2007).

The rejections of independent claims 8 and 20 fail to satisfy a prima facie case of obviousness as enunciated in Takeda. It is flawed logic to allege that simply because other bile acids are amenable to modification by a sample synthetic strategy that the reference provides adequate support for using un-C(3)-functionalized bile acids as biologically functional agents for the instantly claimed use. It is well recognized in the art that chemical synthetic strategy does not predict or suggest biological function. The Examiner's assertion is akin to claiming that the

process of oxidizing a benzyl ring by a particular mechanism suggests that the resulting phenol will lower cholesterol- it will not.

Examiner asserts that the above fact "is immaterial" and that "Applicant has presented no reason or evidence why one of ordinary skill would not expect the invention of Niedzinski to function with other C(3) bile acid conjugates, or for that matter with other bile acid conjugates corresponding to Niedzinski's C(24) conjugates." (Paper No. 20070907, pg. 10). The provocative assertion found in Paper No. 20070907 on page 9 that Niedzinski does not require derivatization at the C(3) position is a gross mis-interpretion of the reference and steroid chemistry nomenclature. First, Niedzinski does not teach the activity of any C(24) conjugate in the absence of C(3)-functionalization. Second, in Niedzinski the only modification to C(24) is alkyl esterification, and a teaching of relevance to DNA binding domains at C(24) is simply not present per the pending claims. Third, a proper analysis of the scope of the instant claims makes clear that the C(3) position is unmodified in all members of the claimed group. Thus, it is immaterial that C(3)-functionalized cholic acid may function similarly to other C(3)-functionalized bile acids because the instant invention does not claim any C(3)-functionalized bile acids. To interpret the pending claims otherwise negates the specific Markush group of A-R_1 since derivatizing at C93) would render the group members equivalent. Thus, Niedzinski does not "'suggest making the specific molecular modifications necessary to achieve the claimed invention'" Takeda, 83 USPQ2d at 1174 (quoting In re Deuel, 51 F.3d 1552, 1558 (Fed. Cir. 1995) (internal references omitted). The broadest reasonable interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. In re Cortright, 165 F.3d 1353, 1359 (Fed. Cir. 1999). A person skilled in the art readily recognizes that in order for A-R_1 to be any of the claimed group that modification of C(3) must be absent.

Moreover, a person having ordinary skill in the art recognizes that Niedzinski is limited to teaching that both C(3)-functionalization and a C(24)-allyl group specifically on cholic acid creates a molecule that when used in as an additive to other transfection agents enhances or inhibits delivery of conjugated DNA in digestive fluid- not that Niedzinski's molecules are biologically functional equivalents to the un-C(3)-functionalized molecules used in the instantly claimed invention. Niedzinski teaches merely that: "Co-formulation of these lipids did not compromise the gastroprotection of DNA imparted by a lipoplex preparation. These modified lipoplexes were also shown to be active in a transfection experiment." (page 726, second column, first full paragraph.) (emphasis added) Thus, it was the modified co-formulations of C(3)- and C(24)-functionalized cholic acid combined with common transfection lipids that were active as transfection agents. A person having ordinary skill in the art recognizes that Niedzinski offers no teaching or suggestion that C(3)- and C(24)-functionalized cholic acid is suitable as a transfection agent alone, let alone any suggestion that un-C(3) functionalized bile acid derivatives of the instant claims are functional in the absence of common transfection agents. Indeed, an ordinary practitioner recognizes that had the C(3)- and C(24)-functionalized cholic acid of Niedzinski been recognized to be functional transfection agents on their own that there would be no need to supplement them with known active common transfection agents as Niedzinski did. In constrast the the prior art, the claimed compounds are effective in transfection absent added liposomes per Fig. 6 of the instant application .

Keener further fails to suggest the instant invention as the cholesterol derivatives of Keener are not functional equivalents of the C(3)-functionalized cholic acid derivatives of Niedzinski nor of the compounds of the instant claims. The bile acids of Keener are not known material based on suitability for intended use as Niedzinski teaches that suitability for delivery of

DNA to cells requires both a C(3)-functionalized group and co-administration with synthetic lipids. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on Applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958). As the compounds of Keener are not equivalents of Niedzinski, the combination of Niedzinski and Keener does not teach or suggest the use of non-C(3)-functionalized cholesterol derivatives alone as suitable for delivery of DNA to cells as is claimed in the instant invention.

As there is no teaching or suggestion in either the cited prior art or the cited knowledge in the art to use un-C(3)-functionalized bile acids to deliver nucleic acid to target cells, a prima facie case of obviousness under 35 U.S.C. §103 as defined by KSR and Takeda has not been met.

Argument 2: Niedzinski and Keener in view of Gebeyehu fails to render the A-R_1-Q-Z or A-R_1-Q-Y-Z moieties obvious in the instant inventive method.

The further teaching of Gebeyehu also fails to sustain a prima facie case of obviousness. Gebeyehu is referred to on page 11 of Paper No. 20070907:

> Regarding Gebeyehu, Applicant argues that the reference does not teach or suggest the use of any cholesterol derivative other than stigmasterol, ergosterol, or cholic acid. Gebeyehu was not relied upon to teach any derivative other than these. The cholesterol derivatives are taught by Niedzinski and Keener. Gebeyehu taught the use of nucleic acid binding domains, such as a polyamine or a polycationic peptide, in combination with a steroid such as cholic acid, stigmasterol, or ergosterol, and a linker. Clearly polyamines and cationic peptides were recognized in the art as equivalents as DNA binding domains in delivery compositions, such that it would have been obvious to substitute one for the other in the invention of Niedzinski as modified by Keener.

Thus, Gebeyehu is cited merely for the proposition that polyamines and cationic peptides are art recognized equivalents. (*see also* Paper No. 20070907, pg. 5.) The failure to make a prima facie case of obviousness based on Niedzinski in view of Keener is not corrected by any teaching or suggestion in Gebeyehu. In sum, Niedzinski in view of Keener in further view of Gebeyehu fails to establish a prima facie case of obviousness for all elements of the instantly claimed invention.

B. The rejection of claims 15 and 16 under 35 U.S.C. §103(a)

That the nucleic acid of Perrie may be a therapeutic product is of no import to suggesting the conjugating agent of the instant claims in light of the shortcomings of Niedzinski, Keener, and Gebeyehu. Appellant submits that claims 15 and 16 are allowable on the basis of dependency from an allowable base claim and incorporates in its entity the above remarks regarding Niedzinski in view of Keener and Gebeyehu in that, alone or in combination, they are deficient in rendering obvious the claimed invention.

Perrie is cited in support of a rejection of claims 15 and 16 because "the nucleic acid of Perrie is considered to be a therapeutic product that is antibiotic in nature by virtue of its activity in inducing an immune response against hepatitis B virus." (Paper No. 20070907, pg. 7.) Mere suggestion that a nucleic acid may be used as a therapeutic product does not suggest the structure or function of the conjugating agents of the subject claims to one having ordinary skill in the art. Further, Perrie et al. is limited to teaching oral administration of a liposome entrapped plasmid DNA molecule and that DNA by entrapment into liposomes is essential to its protection. (p. 186, Introduction; p, 190.) Niedzinski supports Perrie by teaching function of cholate amphiphiles when used as additives to liposomes. However, neither Perrie nor the cited prior art teach or

suggest the conjugating agent of the instant claims as part of a pharmaceutical composition with or without a therapeutic compound.

As such, Niedzinski in view of Keener and Gebeyehu, in further view of Perrie fails to establish a prima facie case of obviousness for all elements of the instantly claimed invention.

C. The rejection of claims 11, 12, 15, and 16 under 35 U.S.C. §103(a)

It is absurd to conclude that because C(3)- and C(24)-functionalized cholic acid does not "appear to compromise the gastroprotection afforded by lipoplex formulation with DNA," that Niedzinski teaches or suggests to a person having ordinary skill in the art that the C(3)- and C(24)-functionalized cholic acid can substitute for any cationic lipid such as the LIPOFECTIN reagent of Kitadai. (Niedzinski, pg. 725, paragraph bridging columns 1 and 2.) (emphasis added) In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on Applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958).

Appellant submits that claims 11, 12, 15, and 16 are allowable on the basis of dependency from an allowable base claim and incorporates in its entity the above remarks regarding Niedzinski in view of Keener and Gebeyehu in that, alone or in combination, they are deficient in rendering obvious the claimed invention.

Kitadai is cited as teaching that "[t]ransfection was performed using the cationic lipid formulation LIPOFECTIN (DOTMA/DOPE)." (Paper No. 20070907, pg. 8.) Neither this nor any other teaching of Kitadai corrects the above shortcomings of Niedzinski, Keener, and Gebeyehu. There is no suggestion in Niedzinski, Keener, Gebeyehu or Kitadai to substitute

C(3)-functionalized cholates for the LIPOFECTIN of Kitadai, nor does the cited prior art contain a suggestion that the C(3)-functionalized cholates of Niedzinski are capable of substituting for the LIPOFECTIN of Kitadai. Indeed, all biological, protective, and delivery functionality in Niedzinski is taught in the presence of the transfection agent DOTAP, DOPE, or DMDHP. These results are summarized as "the addition of the cholate lipids does not appear to compromise the gastroprotection afforded by lipoplex formulation of DNA." (Niedzinski, pg. 725.) Further, Niedzinski teaches nucleic acid delivery to target cells using DOPE and DMDHP encapsulating molecules where "DMDHP was selected for the transfection experiments based on the superior transfection activity exhibited by DMDHP." (Niedzinski, pg. 725.) All results in Niedzinski are to stimulate or inhibit the transfection activity of DMDHP. Niedzinski concludes that "cholate 5 may be suitable for addition to a therapeutic lipoplex preparation." Id. (emphasis added) Thus, a person having ordinary skill in the art recognizes that Niedzinski teaches addition to, not substitution for transfection agents disclosed therein or those of Kitadai. As such, Kitadai fails to correct the shortcomings of Niedzinski in view of Keener and Gebeyehu.

Regarding claims 15 and 16, that the nucleic acid Kitadai may be a therapeutic product is of no import to suggesting the conjugating agent of the instant claims in light of the shortcomings of Niedzinski, Keener, and Gebeyehu.

Conclusion

In summary, Examiner's references and combination of references that make up the outstanding rejections fail to establish a prima facie case of obviousness by neither teaching nor suggesting to a person having ordinary skill in the art the subject conjugating agents or their suitability for nucleic acid delivery to a cell.

Accordingly, the obviousness rejection under 35 U.S.C. §103(a) with regard to claims 1-

7, 9, 10, 13-18, 20, 21, and 24 should be REVERSED. Similarly, the obviousness rejection under 35 U.S.C. §103(a) with regard to claims 15 and 16 should likewise be REVERSED. Also, the obviousness rejection under 35 U.S.C. §103(a) with regard to claims 11, 12, 15 and 16 should be REVERSED.

VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as Appendix A. As indicated above, the claims in Appendix A include all the amendments filed by Appellant.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 07-1180, under Order No TSR-10002/38.

Dated: January 22, 2008

Respectfully submitted,

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APPENDIX A

CLAIMS ON APPEAL

1-7 (Canceled)

8. A method of nucleic acid delivery to target cells of a subject comprising the step of administering a conjugating agent-nucleic acid complex where the conjugating agent comprises A–R_1–Q–Z; where A-R_1 is a cholesterol derivative selected from the group consisting of cholestanol, coprostanol, glycocholic acid, chenodeoxycholic acid, desoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, and taurochenodeoxycholic acid, where Q is a sulfur, or oxygen; and Z is a polyionic peptide.

9. The method of claim 8, wherein said administration is oral.

10. The method of claim 8, wherein nucleic acid of said complex is expressed as a protein in said target cells.

11. The method of claim 10 wherein said protein is secreted from said target cells.

12. The method of claim 10 wherein said protein is of a class selected from the group consisting of: proteases, pituitary hormones, protease inhibitors, growth factors, cytokines,

somatomedians, chemokines, immunoglobulins, gonadotrophins, interleukins, chemotactins, interferons, and lipid-binding proteins.

13. The method of claim 8 wherein nucleic acid of said complex is selected from the group consisting of: DNA, RNA, mRNA, miRNA, ribozyme, and antisense sequences.

14. The method of claim 8 wherein said complex is administered as part of a pharmaceutical composition.

15. The method of claim 14 wherein said pharmaceutical composition comprises an active therapeutic compound.

16. The method of claim 15 wherein said therapeutic compound is selected from the group consisting of: an antibiotic, a gamma or beta radiation emitting species, an anti-inflammatory, an antitumoral, an antiviral, an antibody, a hormone, an enzyme, antigenic peptide and antigenic protein.

17-18. (Canceled)

19. The method of claim 8, wherein said target cells are gastrointestinal cells.

20. A nucleic acid delivery composition comprising a conjugating agent-nucleic acid complex having the formula:

$A—R_1—Q—Y—Z$

where $A\text{-}R_1$ is a cholesterol derivative selected from the group consisting of cholestanol, coprostanol, glycocholic acid, chenodeoxycholic acid, desoxycholic acid, glycochenodeoxycholic acid, taurocholic acid, and taurochenodeoxycholic acid; where Q is sulfur, or oxygen; where Y is a linker peptide having a negative, neutral, or positive charge; and where Z is a polyionic peptide.

21. (Canceled)

22. The composition of claim 20 wherein said cholesterol derivative is a deoxycholic acid.

23. (Canceled)

24. The composition of claim 20 wherein said Q is oxygen.

25. (Canceled)

26. The composition of claim 20 wherein Z is polycationic.

27. The composition of claim 26 wherein Z contains at least six residues.

28-29. (Canceled)

30. A commercial package comprising a composition of A–R_1–Q–Z according to claim 8 as an active ingredient together with instructions for the use thereof as a nucleic acid delivery agent to a subject.

APPENDIX B

EVIDENCE

There is no evidence that has been entered or relied upon in this appeal.

APPENDIX C

RELATED PROCEEDINGS

There are no decisions that have been rendered by a court or the Board in any proceeding identified in the related appeal.